Epitomes

Important Advances in Clinical Medicine

Anesthesiology

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The Council on Scientific Affairs of the California Medical Association presents the following epitomes of progress in anesthesiology. Each item, in the judgment of a panel of knowledgeable physicians, has recently become reasonably firmly established, both as to scientific fact and clinical importance. The items are presented in simple epitome, and an authoritative reference, both to the item itself and to the subject as a whole, is generally given for those who may be unfamiliar with a particular item. The purpose is to assist busy practitioners, students, researchers, and scholars to stay abreast of progress in medicine, whether in their own field of special interest or another.

The epitomes included here were selected by the Advisory Panel to the Section on Anesthesiology of the California Medical Association, and the summaries were prepared under the direction of Dr Jackson and the panel.

New Muscle Relaxants

FOUR NEW MUSCLE RELAXANTS have recently been introduced into clinical practice. These muscle relaxants must be considered in comparison with atracurium besylate and vecuronium bromide, two effective drugs that have an intermediate duration of action, little cardiovascular effect, and a low incidence of postoperative residual weakness. Pipecuronium bromide and doxacurium chloride have a long duration of action, similar to tubocurarine chloride and pancuronium bromide, but without their cardiovascular effects of hypotension and tachycardia, respectively. The cardiovascular safety is excellent, but no better than that of vecuronium. The difficulty of rapidly antagonizing neuromuscular block produced by pipecuronium and doxacurium with consequent persistent postoperative weakness makes them less cost-effective than the intermediate-duration drugs for most surgical situations. Their long duration of action may be of value during long operations, where patients' tracheas will remain intubated postoperatively, or in intensive care units.

Mivacurium chloride is the only short-acting, nondepolarizing muscle relaxant, as it is hydrolyzed by plasma cholinesterase. Intubating doses can stimulate histamine release and, in doses of 0.2 mg per kg or more, may produce hypotension with an incidence similar to that of atracurium. Neuromuscular function following intubating doses begins to recover in 10 to 15 minutes. For procedures longer than 30 minutes, mivacurium is best administered by infusion. A guideline for infusion is to start at a rate of 10 μg per kg per minute as soon as there is evidence of recovery from the initial intubating dose, then titrate the infusion rate to the subsequent neuromuscular response. Neuromuscular recovery is rapid even after an infusion of several hours. Full spontaneous recovery after an infusion takes 15 to 20 minutes, and this time is halved by the administration of neostigmine bromide. Mivacurium's duration is substantially prolonged in patients with diminished plasma cholinesterase activity. Its duration is increased by 50% in patients with renal failure and by a factor of 3 in those with severe liver disease. Patients homozygous for the atypical cholinesterase enzyme may be paralyzed for several hours. There is no evidence that patient care is enhanced by using mivacurium versus the intermediate-duration drugs vecuronium or atracurium.

The fourth new drug is rocuronium bromide, which has an intermediate duration of action and minimal cardiovascular effects. The pharmacologic advantage of rocuronium is its rapid onset of action. It is the first nondepolarizing muscle relaxant to have an onset that approaches that of succinylcholine chloride. In doses of 0.6 to 0.9 mg per kg, it produces paralysis in 60 to 90 seconds. Its onset is about 50% slower than that of succinylcholine, but intubating conditions at 60 to 90 seconds are similar for both drugs; therefore, rocuronium may be useful for rapid-sequence tracheal intubation. This drug is not a complete replacement for succinylcholine, however, as it does not have an ultrashort duration of action. Rocuronium is priced competitively with vecuronium and atracurium.

The clinical roles of rocuronium and mivacurium have been expanded by a recent notice by the United States Food and Drug Administration (FDA) on succinylcholine's potential to produce sudden, unexpected, hyperkalemic cardiac arrest in children with undiagnosed muscular dystrophy. The FDA has determined that "except when used for emergency tracheal intubation or in instances where immediate securing of the airway is necessary, succinylcholine is contraindicated in pediatric patients." This statement is under review, however, and the contraindication will be revised to a warning. Nonetheless, clinicians who have routinely used succinylcholine to facilitate straightforward elective tracheal intubation in children have been advised to find an alternative. If rapid onset is desired, then rocuronium is an acceptable alternative. If brief duration is paramount, then

mivacurium may be acceptable. Neither drug can be considered a full replacement for succinylcholine, however.

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Preparing Children for Anesthesia and Surgery

IN PREPARING A CHILD for surgery, an anesthesiologist is faced with the unenviable task of separating a starved and frightened child from anxious parents. The scientific rationale for a lengthy preoperative fast has recently been questioned, and based on new studies, preoperative fasting guidelines have been modified. In addition, newer hypnotic drugs and modes of administration can ease the separation of children from their parents.

Whereas the tradition of a preoperative fast can be traced to 1858, decades of studying the epidemiology and risk factors for perianesthetic aspiration of stomach contents have not determined the proper duration of the fast. It has now been established that the gastric fluid of children (older than 1 year) who are allowed to drink clear liquids up until two hours before anesthesia is no greater in acidity or volume than that of children who fast overnight. Therefore, ingesting clear liquids up to two hours before an operation does not appear to increase anesthetic risk. Because substantial physiologic benefit from a shortened fast has not yet been demonstrated, children with esophageal or gastric disease, severe neurologic disease, suffering from pain, receiving narcotics, or presenting airway management difficulties would be likely to benefit from more conservative fasting guidelines. In addition, until more data become available, infants younger than 1 year should fast for three to four hours before a surgical procedure.

The "shot to calm you" is understandably unpopular with children and parents alike. Oral, rectal, or nasal administration of the water-soluble benzodiazepine midazolam hydrochloride is an effective and painless alternative to intramuscular administration. Sedative doses of midazolam when given by these routes range between 0.5 and 1.0 mg per kg. About half of the drug is bioavailable following oral or rectal administration, and the maximal sedative effect will occur within 20 to 30 minutes. Administering the drug nasally increases bioavailability (to about 75%) and provides an even more rapid onset. Because the effects generally dissipate within an hour, recovery from anesthesia is not appreciably prolonged. Oral ketamine hydrochloride, 5 to 10 mg per kg, can be substituted for midazolam; some children may experience unpleasant psychomimetic effects, however, and recovery may be prolonged.

An oral transmucosal form of fentanyl citrate (Oralet) is now available. This consists of a medicated lozenge on a plastic holder. The dose of fentanyl (200 to 400 μg) in each Oralet is substantial, mandating strict adherence to administration and monitoring precautions.

In recent years the preoperative preparation of children for anesthesia and surgery has been reevaluated. Less stringent preoperative fasting guidelines and improvements in preoperative medication techniques have resulted in a less traumatic anesthetic experience without compromising safety.

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Inhaled Nitric Oxide

TREATMENT OF pulmonary hypertension with intravenous vasodilators is limited by systemic hypotension (due to the systemic vasodilator effects of all pulmonary vasodilators) and hypoxemia (due to the reversal of hypoxic pulmonary vasoconstriction). Inhaled nitric oxide (NO) now appears to be a major advance in the therapy for pulmonary hypertension.

Vascular endothelium is able to modulate vascular tone by producing substances that dilate the adjacent smooth muscle. In 1987 NO was identified as endothelium-derived relaxing factor. Nitric oxide produced by the endothelium diffuses into vascular smooth muscle, where it activates soluble guanylate cyclase; the subsequent increase in levels of intracellular cyclic guanine monophosphate produces smooth muscle vasodilation. Endothelium-independent nitrovasodilators such as nitroglycerin and sodium nitroprusside also activate guanylate cyclase, but do so by directly releasing NO. They release NO into both the pulmonary and systemic circulations, so that systemic vasodilation accompanies the pulmonary vasodilation. Nitric oxide itself is rapidly inactivated by hemoglobin in blood, so that the effect of inhaled NO may be localized to the lungs. Thus, inhaled NO diffuses from the alveoli to pulmonary vascular muscle and produces pulmonary vasodilation but no systemic effects. Although NO as a component of air pollution has been considered a toxic gas, it has relatively low toxicity; nitrogen oxides such as nitrogen dioxide that form from NO over time are polluting toxic compounds.

In animals, inhaled NO (5 to 80 parts per million) reverses pulmonary hypertension produced by global hypoxia, thromboxane-mimetic infusion, or heparin-protamine interactions. The pulmonary vasodilation is rapid, completely reversible, and selective, with no